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Summer Undergraduate Research Training in Breast Cancer Imaging

INTRODUCTION

Imaging is used in virtually every cancer patient, in many animal models of cancer, and in a large number of in vitro cancer-related experiments. Imaging research is thus fundamental to advanced cancer research. The medical physics program at the University of Chicago is recognized internationally for its research excellence and for its training of investigators at the pre-doctoral and post-doctoral level. Many of the trainees go on to careers in cancer research. We believe that exposure and immersion of undergraduate students in summer research in breast cancer imaging is expected to provide a forum for establishing a set of next-generation researchers who will pursue breast cancer research via Ph.D. or Ph.D./M.D. programs as their career. Six undergraduate students participate in research in breast cancer imaging at the University of Chicago within the laboratory and administrative structure of the well-established Graduate Programs in Medical Physics. Six summer students in the Summer 2003 quarter learned and experienced research in breast cancer imaging through didactic lectures, hands-on research, interactive research project meetings, formal research seminars, and in the writing and oral presentation of their research. All four of the mentors who participated as primary summer advisors in the grant (Giger, Halpern, Jiang, and Nishikawa) have a long history of breast cancer research and funding. In addition, the summer students have attended research presentations of others in the labs (such as post-doctoral fellows, graduate students, and faculty) and each presented their research at the end of summer to researchers at the University of Chicago.

ACCOMPLISHMENTS

Six students participated in the summer undergraduate training in breast cancer imaging during the Summer of 2003. Each student was assigned to one of the four investigators on the grant (Giger, Nishikawa, Jiang, or Halpern) and performed research in their lab. In addition, the students participated in day tours to other faculty labs as well as in clinical areas such as breast MRI, diagnostic breast imaging, and CT. The students' research and accomplishments are listed below for each student.

1. Petrice Mostardi, Vanderbilt University (Advisor: M. Giger)

The field of computer-aided diagnosis (CAD) is rapidly growing, especially in the area of the detection and diagnosis of lesions in breast images since the earlier breast cancer is found the better the prognosis for the patient. While in the lab, Petrice increased her knowledge of medical imaging through the reading of books on mammography, image processing, and medical physics, and through various discussions with me. She learned about scientific investigations and the corresponding need for creativity and rigor. In the lab, Petrice was involved in the collection and digitization of radiographic films for a mammography database and assisted in an investigation on computer-extracted features of mammographic lesions and parenchyma for the prognostic assessment of breast cancer cases. From this research, we developed a computerized image analysis method that outputs an estimated probability of a breast cancer case being lymph node positive. We demonstrated that axillary lymph node involvement in breast cancer patients may be related to computer-extracted mamographic features of the lesions and the surrounding parenchyma. During the summer, Petrice learned about computer vision, linear discriminant analysis, and ROC analysis as well as the clinical aspects of radiology including mammography and chest radiography. Her contributions resulted in co-authorship of a presented abstract at the 2003 RSNA meeting. Petrice is now looking into graduate schools and medical schools for MSTP programs and radiological imaging.

2. Andrew Liu, John Hopkins (Advisor: M. Giger)

During Andrew's summer training, he increased his knowledge of medical imaging through the reading of books on mammography, image processing, and medical physics, and through various (at times daily) discussions with me. He also learned about scientific investigations and the corresponding need for creativity and rigor. While his thirst for new knowledge was extremely large (as compared to other summer students), he did not hesitate to take the time to explain mathematical concepts and computer coding to others. The research on which Andrew worked involves the assessment of lesion segmentation by means of evaluating the effect on overall system performance in the task of distinguishing cancer and non-cancerous breast

lesions. Basically, if the breast lesion is not accurately segmented from the background in the mammogram, then the corresponding computer-extracted lesion characteristics (that depend on accuracy of the lesion margin) and the subsequent discriminant analysis could be miscalculated. Andrew ran the computerized lesion segmentation programs on approximately 300 images, and wrote Perl and Matlab computer programs to assist in the comparison of characterization results. He also coded methods with which to pre-process the medical image in order to enhance the lesion segmentation.

3. Phillip Smithback, University of Chicago (Advisor: H. Halpern)

During the summer training, Phil Smithback enhanced his knowledge of electron paramagnetic resonance (EPR) imaging. He worked on initiating the upgrade of a EPR spectral line fitting program. He also assisted in documenting how our current fitting program works. Phil's flowchart is currently aiding us now in upgrading the fitting program. Phil also worked on the assembly of a large, high homogeneity low field electromagnet. His contribution included not only the muscle but insight into the optimum placement of these coils to help work out some of the manufacturing imperfections. He actively participated in the EPR imaging of oxygen in tumors of mice and developed some competence in working with these creatures. He learned the basics of EPR and developed competence in the set up and use of the imager.

4. Jeremy Schmidt, Yale University (Advisor: R. Nishikawa)

Jeremy worked on two projects. The first was to digitize mammograms for two different observer studies. The first observer study is to measure the improvement in radiologists' ability to detect breast cancer when aided by a computer-aid detection (CADe) scheme. In this study, we are using cases where the cancer was originally missed at screening mammography. The second observer study is to demonstrate that radiologists reading times will decrease when they use a CADe scheme when viewing mammograms on softcopy display, where the CADe will obviate the need to zoom and pan the image. Four-hundred cases were digitized for the first study and an additional 100 cases were digitized for the second study.

Jeremy also measured the temporal stability of film digitizers. For computer-aided diagnosis systems to be developed and to be implemented clinically, screen-film mammograms need to be digitized. The stability of the digitizer is important if these systems are to work well clinically. A test film was digitized daily for a period of 50 days on two different Lumisys 85 digitizers. The test film had a step image containing 21 different film optical densities. The pixel value of steps 1, 10, 12, 13, and 19 were recorded and the mean and standard deviation values were computed for the 50 different measurements.

Jeremy found that the variation in pixel value was small at all steps (different film optical densities). The coefficient of variation was approximately 1%, compared to 2% for a full-field digital mammography system and approximately 5% for the film processor (used to develop the exposed film). Jeremy was also able to identify that one of the digitizers needed to be repaired by comparing the mean pixel values as a function of step number for the two digitizers. The defective digitizer had consistently lower mean values at high optical densities. These results will be incorporated into the dissertation of Laura Yarusso, a Ph.D. candidate.

5. Jill Schmitz, Hastings College (Advisor: R. Nishikawa)

Jill worked on characterizing the physical characteristics of film digitizers in our laboratory. As part of our effort in developing computer-aided diagnosis systems, we digitize film mammograms to get a digital image. The process of digitizing a film can degrade the image. It is important to measure the characteristics of the digitizer to understand if and when this will occur.

Jill measured the characteristic curve (pixel value versus film optical density) and the noise power spectrum (NPS) of three different Lumisys 85 digitizers. Standard methodologies were used. The NPS were measured using a number of uniformly exposed films each having a different optical density ranging from 0.25 to 3.5.

All three digitizers had a linear response to a range of optical densities up to 3.5. There were small differences in the slope of the characteristic curves of the three digitizers. The noise power spectra were fairly flat between 0.5 and 10 cycles/mm, with about a 1-decade drop in noise power at the highest frequencies. Below about 0.5 cycles/mm there was a marked increase in noise power by 1-2 decades depending on the film density. The cause of this increase is unknown. The noise of the digitizer increased monotonically with increasing film density with a large increase between 3.0 and 3.5 optical density. This is due to the electronic noise of the digitizer, which becomes dominant at low light levels. The noise of the digitizer is smaller than the noise of the screen-film system (due to x-ray quantum noise and film granularity) for optical densities less than approximately 2.5. At optical densities above 3.0, the noise of the digitizer will be greater than the noise of the screen-film system.

6. Nicole G. Lunning, University of Chicago (Advisor: Y. Jiang)

Nicole took part in an effort to assemble a database of full-field digital mammograms for CAD research. Notably she has helped salvage about 100 cases of "orphan" mammography studies to the clinical PACS system. Database collection and analysis requires careful organization in order to allow for training and testing of CAD classifiers. Nicole's effort has helped research in CAD and FFDM. Her efforts resulted in co-authorship in a presentation at AJR.

KEY RESEARCH ACCOMPLISHMENTS

1. An ongoing summer undergraduate research program in breast cancer imaging has now been established at the University of Chicago, under the direction of M. Giger who also directs the graduate programs in medical physics.
2. The competitive program is limited to 6 undergraduate slots per summer and has successfully trained 6 students during the summer of 2003.
3. Undergraduate students are learning the rigors of research and are contributing to a level that allows for co-authorship on presentations and future papers.
4. Evidence of the influence of the program is shown through the education/career choices of the students with P. Mostardi considering MD/PhD programs in radiological imaging and A. Liu in biomedical engineering.

REPORTED OUTCOMES

1. Bonta, I, Giger, ML, VybornyCH, Heimann R, **Mostardi P**, Li H, Lan L:
Prognosis of breast cancer patients based on computerized
mammographic analysis. Abstract presented at RSNA, December,2003.
2. Rana RS, Jiang Y, Schmidt RA, Liu B, Sennett AS, Chambliss J, Abe H,
Lunning NG: Independent Evaluation of Computer Classification of
Malignant and Benign Calcifications in Full-Field Digital Mammograms.
Abstract presented at 104th Annual Meeting of the American Roentgen
Ray Society, Miami Beach, Fl, May, 2004.

CONCLUSIONS

We have established a formal summer undergraduate research program in breast cancer imaging at the University of Chicago. The students are being exposed to various laboratories and clinical areas as well as being immersed in a focused research project. They also have attended various presentations by post-doctoral fellows, graduate students, and faculty during the summer. The six summer students in the Summer 2003 quarter learned and experienced research in breast cancer imaging through didactic lectures, hands-on research, interactive research project meetings, formal research seminars, and in the writing and oral presentation of their research. All four of the mentors (Giger, Halpern, Jiang, and Nishikawa) participated as primary summer advisors in the grant.

With the start of summer 2004, we received multiple applications for the summer undergraduate research training program, however we have accepted only six for the funded slots.